REMARKS

This is in response to the Office action dated February 22, 2006. Claims 18, 20, and 21 are currently pending in this application. As an initial matter, the undersigned wishes to thank the Examiner for the courtesy extended to him during today's telephone interview. During the interview, independent claim 18 was discussed in detail. Also discussed were the rejections under 35 USC § 112, the prior art rejections, including (briefly) each of the references: Liu et al, Engel et al, and Yan et al., and the amendment to claim 18.

As discussed, claim 18 is being amended to delete the limitation that "the amine is not an alpha-amino acid. As amended, claim 18 recites:

> 18. A method for producing an amine from a target ketone, comprising:
>
> creating a mutated enzyme that catalyzes reductive amination of the target ketone; and
>
> providing the mutated enzyme in a reaction mixture comprising the target ketone under conditions sufficient to permit the formation of the corresponding amine to thereby produce the amine,
>
> wherein the ketone is not a 2-ketoacid.

No new matter is added by the amendment. Indeed, the present amendment deletes the phrase "[wherein] the amine is not an alpha-amino acid" introduced in an earlier amendment. As discussed at length during the interview, support for the claim limitation, "wherein the ketone is not a 2-ketoacid," is found throughout the specification and the abstract. See in particular the following passages:

1. Abstract, page 29, lines 9-11:

"The methods comprise creating a mutated enzyme that catalyzes the reductive amination . . . of the target 2-ketoacid or ketone . . . and providing the mutated enzyme in a reaction mixture comprising the target 2-keytoacid or ketone . . ."

(Emphasis added.)

2. Summary of the Invention. Compare the bottom paragraph of page 3, carrying over to the top of page 4:

"In one embodiment, the invention is directed to a method for the production of an amino acid from a target 2-ketoacid . . ."

with the first full paragraph of page 4, lines 5-9:

"In another embodiment, the invention is directed to a method for the production of an amine from a target ketone."

3. Detailed Description, page 4, lines 33-34 (distinguishing between a ketone and a 2-keto acid); and especially page 5, bottom paragraph:

"As used herein, 'target compound' refers to a substance that is desired to be acted upon by an enzyme as a substrate. Typical target compounds include. . . ketones, . . . ketoacids. . ., and the like."

Additional support is also found at pages 9 and 10, particularly Scheme 3 and the discussion on the bottom paragraph of page 9 (distinguishing between a ketone and a ketoacid).

Hence, the specification as filed plainly distinguishes between ketones and 2-ketoacids, and provides support for the previously amended claim language, "wherein the ketone is not a 2-ketoacid."

Consider now the rejections under 35 USC § 112. As amended, claim 18 recites a method for producing an amine from a target ketone, in which two steps are recited: creating a mutated enzyme that catalyzes reductive amination of the target ketone, and providing the mutated enzyme in a reaction mixture comprising the target ketone under conditions sufficient to permit the formation of the corresponding amine, to thereby produce the amine, with the additional limitation that the ketone is not a 2-ketoacid. This language is definite and, as discussed during the telephone interview, readily understood by a person having ordinary skill in the art, as well as by potential infringers.

As a hypothetical example, one could take an existing enzyme, e.g., a dehydrogenase, and test its ability to reductively aminate any of a number of ketones, other than a 2-ketoacid. Unsurprisingly, the inability of the enzyme to catalyze the reductive amination will be noted. Per the invention, however, one can take that enzyme, create a mutated version of the enzyme (using, e.g., any of the methods described in the specification), and test the ability of the mutated enzyme to catalyze the reductive amination of the target ketone. If the test is positive, one knows that the desired mutation was achieved, and the enzyme can then be used as a catalyst for converting the target ketone into its corresponding amine. The particular method of creating the mutated enzyme -- mutagenesis, shuffling, molecular breeding, or gene assembly (described in the specification at page 2 lines 13-24, at page 5, lines 6-9, and in the examples beginning on page 11), or even subsequently developed methods of creating mutated enzymes -- is irrelevant to infringement of claim 18 and the claims dependent there from.

The specification provides several examples of creating mutated enzymes, testing their ability to catalyze the reductive amination of various amines, and then using the mutated

enzymes to facilitate the reductive amination of the target ketones to produce their corresponding amines.

Claim 20 was similarly rejected under § 112, presumably for depending from a rejected base claim (18). Applicant submits that it, too, is definite and allowable. Claim 21 is also rejected, with the Examiner stating, at the bottom of page 5 of the Office action, "[c]laim 21 is not understood where one would not likely provide an enzyme that does not exist. Such enzymes likely exist in an organism. Further, it is directed to mutating an enzyme but does not set forth how it is mutated."

Claim 21 depends from claim 18, and like 18, calls for the creation of a mutated enzyme and the use of the enzyme to catalyze the reductive amination of a target ketone under conditions sufficient to permit the formation of the corresponding amine. Claim 21 adds the additional limitation that one starts with a particular type of enzyme, namely, an amino acid dehydrogenase. A mutated enzyme is then created by mutating the existing amino acid dehydrogenase. In addition, the claims calls for the mutated enzyme to catalyze the reductive amination of the target ketone at a greater rate than the existing amino acid dehydrogenase.

Like claim 18, claim 21 is readily understood by a person having ordinary skill in the art. In this case, the starting point is an "existing" enzyme -- specifically an amino acid dehydrogenase. It is used to create a mutant enzyme. The mutant enzyme catalyzes reductive amination of a target ketone at a rate faster than that achieved by the existing enzyme.

A number of embodiments are within the scope of claim 21. For example, in one embodiment. the amino acid dehydrogenase does not catalyze reductive amination of the target ketone (but may well catalyze reductive amination of some other compound). The rate at which the so-called "existing enzyme" catalyzes reductive amination of the target ketone would, therefore, be zero. Per claim 21, however, the existing enzyme is used to create a mutated enzyme, which catalyzes, and is used to catalyze, the reductive amination of the target ketone at a rate higher than zero. In another embodiment, the amino acid dehydrogenase catalyzes

reductive amination of the target ketone, but only slowly. Per claim 21, the starting amino acid dehydrogenase is mutated such that the resulting mutated enzyme that is created catalyzes reductive amination of the target ketone at a greater rate than does the starting amino acid dehydrogenase.

Independent claim 18's recitation of "creating a mutated enzyme," therefore envisions a number of possibilities, including synthesis of the mutant enzyme *de novo*, as well as starting with an existing enzyme, which is then mutagenized to produce a mutated enzyme having the desired properties, namely, the ability to reductively aminate a target ketone (other than a 2-ketoacid) to form an amine, at a rate faster than that achieved with the original enzyme. Claim 18 encompasses both of these scenarios, whereas claim 21 encompasses the latter scenario.

Consider now the prior art rejections. Liu et al teaches the use of L-amino acid deaminase to catalyze the conversion of L-amino acids to alpha-ketoacids, which then serve as substrates for D-amino acid transaminases, and are thus converted to the D-amino acids. The reference does not describe the reductive amination of ketone to an amine, as recited in Applicant's claims.

Engel et al describes the screening of amino acid dehydrogenase and the modification of amino acid dehydrogenase from mutants, but does not teach or suggest the reductive amination of ketones to form an amine.

Yan et al discloses making mutant enzymes, but does not teach making mutants that catalyze the reductive amination of a ketone to an amine, let alone a ketone that is not a 2-ketoacid.

In short, the references, whether taken alone or in combination, do not teach or suggest the presently claimed invention, which calls for (a) creation of a mutant enzyme capable of catalyzing the reductive amination of a target ketone, and (b) use of that mutant enzyme to

facilitate the reductive transformation of a ketone, other than a 2-ketoacid, to its corresponding amine.

Accordingly, Applicant respectfully submits that this case is in condition for allowance. If the Examiner feels that additional clarification is needed, he is invited to contact the undersigned by telephone at his earliest convenience.

Respectfully submitted,

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